Supercoil dynamics along stretched DNA by Brownian dynamics

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Abstract

DNA supercoiling is an often overlooked participant in essential cellular processes including transcription, replication and recombination. Supercoils are both a byproduct of and a significant input to these processes. For example, RNA polymerase molecules binding negatively supercoiled DNA and producing positive supercoiling ahead of (and negative supercoiling behind) the transcription site. Studies on thermal fluctuations and DNA-protein interactions, supercoils are dynamic structures which accumulate, separate, translate, and dissipate. Recent single molecule studies have observed the dynamic formation, diffusion, hopping, and dissipation of supercoils. Here, we employ coarse-grain Brownian dynamics simulations, parallelizing recent experiments, to build understanding beyond the capabilities of current experimental techniques. Our computational model incorporates hydrodynamic interactions, thermal fluctuations, bending, torsion, extension, and electrostatics. We perform many simulations including trajectories of 21 kilo-basepair lengths of supercoiled DNA spanning up to about 100 ms. We observe several quantities describing the dynamics of supercoils, including: the average number of supercoils, their lifetime, first juxtaposition time, and diffusion constants.

SM experiments capture plectoneme dynamics [2]
- Diffusion and hopping
- Diffraction limits resolution of supercoiled structures

Distribution of first juxtaposition times
- Time for two sites on a DNA molecule, separated by a distance \( L_{sep} \), to approach each other to within a distance of 10 nm. See, for example [5, 6]

Results

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- Time for two sites on a DNA molecule, separated by a distance \( L_{sep} \), to approach each other to within a distance of 10 nm. See, for example [5, 6]

Observations

- Plectoneme dynamics occur on time scales larger than about 100 ms
- Computationally predicted diffusion constant is about 0.3 to 0.5 \( \mu m^2/s \)
- Accounting for hydrodynamic interactions appears to make minor impact on diffusion

Future Directions

- Reduce computation time
- Run longer simulations with hydrodynamic interactions
- Characterize plectoneme hopping [2]
- Account for sequence dependent stiffness and intrinsic curvature

References


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